



KDIGO Controversies Conference on Maintaining Kidney Health and Preventing CKD

Breakout Group Questions

Breakout Group 1: The Case for Kidney Health

Goal: Define CKD prevention, consider its integration within a wider prevention ecosystem, and identify endpoints to assess the impact of prevention strategies and interventions

- **CKD current definition and shortcomings**
 1. Do treatable pathogenic events pre-date the current eGFR or albumin-creatinine ratio (ACR) threshold values used to diagnose CKD?
 2. How can we define the syndromic nature of obesity, metabolic syndrome, diabetes, and cardiovascular-kidney disease to promote early diagnosis for prevention and treatment?
 3. Are there studies showing outcomes by CKD assessment, i.e., one-time eGFR versus repeat measures within 90 days, spot-urine ACR versus persistent, eGFR or ACR only?"

- **Definition of primary prevention of CKD**
 1. What are the most accurate ways and nomenclature to describe prevention of CKD and the possibility of CKD reversal?
 2. Do we need a nomenclature that clearly identifies CKD prevention as conceptually different from CVD prevention?
 3. How do we differentiate primary prevention of CKD from secondary prevention of CVD for research and implementation?
 4. How do we conceptually integrate primary prevention into a wider prevention ecosystem of primordial and secondary prevention of CKD?
 5. How should lifestyle interventions be implemented in primordial CKD prevention? What research is needed? What population would benefit most?

- **Assessing the success of a primary prevention intervention**
 1. Can we use ACR maintained in A1/A2 and GFR categories 1/2 with stable eGFR decline $<1 \text{ ml/min per } 1.73^2$ within a certain time frame as a definition of prevention or remission of CKD (similar to remission of diabetes)?
 2. Are there biomarkers besides cystatin C that improve the predictive value of ACR, serum creatinine, and cystatin?
 3. How can standardization of biomarkers move forward faster?
 4. Why is cystatin C not used routinely as a replacement for (or in addition to) serum creatinine?
 5. Can we use major adverse kidney events (MAKE)? If so, which ones? 40 or 50% decrease in eGFR? Doubling of serum creatinine or kidney failure or kidney death?
 6. Given that kidney failure is a rare outcome early in the disease process, should risk models for CVD also be used to assess CKD prevention (i.e., CVD outcomes as CKD complications)?
 7. Since proteinuria/albuminuria reduction has been used as a surrogate measure for trials in glomerular disease, can these surrogate endpoints and others (e.g., total kidney volume) be more broadly used for ascertaining CKD prevention or regression? If so, what is the appropriate rate of decline? Are there biomarkers (laboratory or histological measures) that can potentially be used to assess CKD prevention (e.g., nephron loss)?

Breakout Group 2: Identifying and Stratifying Individuals for CKD Prevention and Lifestyle Interventions

Goal: Define high-risk populations in different settings (e.g., throughout the lifespan, in the presence of different comorbidities or geographical locations) that may benefit from interventions for preventing CKD

- **Identifying and stratifying individuals for CKD prevention**

1. Should CKD screening be performed in the general population, or should CKD screening be focused on at-risk populations?
 2. If screening is focused on at-risk populations, what factors determine CKD risk now or in the future, e.g., comorbidities, family history, BMI, birthweight, genetic risk scores, hyperfiltration, or others?
 3. Can tools that predict CKD risk efficiently stratify individuals with high CKD risk who should be screened? Are there any novel diagnostic point-of-care instruments or incident CKD risk estimation tools?
 4. What factors should be included in tools that predict CKD risk to stratify CKD screening, especially environmental and occupational factors, in low-resource settings?
 - a. What is the utility of using lifecourse events as primordial factors to identify vulnerable individuals, such as those with family history, suboptimal perinatal development (e.g., preterm birth, low birth weight), major childhood illnesses, or other kidney events (e.g., gouty arthritis, use of NSAIDs)?
 - b. Can we use family history, obesity, and risk scores to identify people who have the highest lifetime risk for developing CKD for regular monitoring and targeted treatment?
 - c. Are there risk scores to predict onset of CKD, and what is their performance and feasibility for implementation?
 5. What level of predicted CKD risk in which timeline should lead to CKD screening recommendations? For example, is a 5% risk in 10 years an indicator for testing?
 6. If screening is focused on at-risk populations, how will clinicians determine CKD risk?
 7. Should CKD risk screening have age limits?
 8. Should CKD risk screening address non-GFR kidney function, e.g., tubular function?
 9. What populations should have follow-up or routine annual CKD or CKD risk screening? For example, following nephrectomy, certain types of chemotherapy, heart failure, others?
- Lifestyle interventions**

1. What is the evidence on the association of lifestyle factors (e.g., diet with high content of red meat/processed foods, sugar-sweetened beverages, foods with high glycemic indexes) and onset of CKD? What are considerations or benefits for protective lifestyles (e.g., plant-based diets, exercise)?
2. What lifestyle interventions should be recommended to reduce CKD risk?
3. What research is needed to identify lifestyle interventions to lower CKD risk?
4. What recommendations should be made regarding environmental causes of CKD (e.g., unknown CKD) to lower population risk for CKD?

Breakout Group 3: Medical Interventions for CKD Prevention

Goal: Assess available evidence on prevention of CKD by medical and non-medical means and define a research agenda to evaluate the clinical effectiveness of novel interventions

□ Pharmacological interventions

1. What is the existing evidence on effective pharmaceutical interventions for CKD prevention?
 - a. What is the evidence for using metformin and renin-angiotensin system inhibitors (RASi) as highly affordable medications in the primary prevention of CKD?
 - b. What is the evidence for using other novel medications in the primary prevention of CKD?
2. What outstanding research is still needed to establish standardized interventions for CKD prevention?
3. Which healthcare professionals are responsible for medication stewardship, particularly regarding avoidance of nephrotoxic agents such as NSAIDs, herbal remedies, and other toxic agents that may negatively impact the kidney?
4. What trial designs (e.g., pragmatic RCT, length of follow-up, outcomes such as GFR thresholds, rates of decline, CKD onset) should be employed

to assess the effectiveness of an intervention for CKD prevention/regression?

- **Procedural interventions (e.g., bariatric, renal denervation) to reduce CKD-related risk factors**
 1. What is the existing evidence to support the effectiveness of procedural interventions to reduce CKD-related risk factors?
 2. What research is still needed to address effectiveness of existing procedural interventions to reduce CKD-related risk factors?

- **Other interventions and devices in treatment-resistant hypertension**
 1. What is the existing evidence to support carotid baroreceptor stimulation?
 2. What is the existing evidence to support renal denervation strategies?

- **Who are the main stakeholders?**
 1. Especially in settings where nephrologists may not be readily available, how can we better engage primary care providers and other allied health partners (e.g., community workers and clinical educators) as primary stakeholders for CKD prevention and regression?
 2. Who are other relevant stakeholders that can assist (e.g., nurses, social workers, pharmacists)?
 3. What do payers need to get involved in an agenda for preventing CKD?

Breakout Group 4: Implementing a Lifespan Approach to Kidney Health

Goal: Identify optimal, cost-effective means for implementing a lifespan approach to kidney health

- **Dissemination and education**
 1. Who are the appropriate audiences for implementing a lifespan approach to kidney health?



2. What is the appropriate timing, cadence, and content for disseminating information to these audiences?
3. Should primary care doctors be certified to highlight their interest and competency in implementing cardiovascular-kidney disease detection, prevention, and treatment programs? How can we better incentivize them?
4. Could CKD-cardiovascular disease competencies or fellowships be used for encouraging the use of multidisciplinary approaches?
5. Can we develop simple tools (similar to diabetes risk scores) to help primary care providers, teachers, and the public to enhance patient activation (i.e., promote self-assessment and self-management)?
6. How can we encourage electronic health record vendors (e.g., Epic, Cerner) to create standardized, non-proprietary CKD care tools (e.g., incident CKD estimation, Tangri kidney failure prognostication, ASCVD 10-yr risk score) that do not require extensive customizations?
7. How can governments or payers (e.g., insurance) be informed to use policies and system approaches to detect and prevent CKD?

□ **Implementation strategies**

1. What key principles should guide the implementation of a lifespan approach?
2. What are the available levers to implement a lifespan approach to kidney health? These might include but are not limited to:
 - a. Public policy, including subsidies
 - b. Government and commercial payers
 - c. Employers and self-insured health plans
 - d. Professional medical societies
 - e. Business sector and industry
 - f. Patient organizations
 - g. Local or regional government agencies
 - h. Philanthropic sources
 - i. Political interest groups
 - j. Social media and other societal influence channels
3. Are there any technological or motivational instruments to facilitate behavioral change?

4. What incentives can be taken to boost adoption of urinary ACR measurements for early intervention?
 - a. What are the barriers and facilitators for measuring urinary ACR?
 - b. Can we bundle the annual measurement of blood pressure, blood glucose, eGFR, and ACR along with BMI and waist to identify high-risk subjects (may add TG/HDL-C), especially in those with primordial risk factors?
5. How can we implement a strategy of intensified control of multiple risk factors (e.g., J-DOIT3) to prevent onset of CKD?
6. What new cost-effectiveness studies are needed to justify early detection of CKD?

□ **Implementation of measurements and benchmarks for recommendations:**

What are the targets?

1. What are the critical early life and socioeconomic determinants that contribute to the development of kidney diseases later in life?
 - a. How can we identify and address these changing determinants to improve kidney health in the long term?
2. Which criteria exist to determine appropriate metrics for evaluating effectiveness of a lifestyle approach to kidney health?
 - a. What are the most effective lifestyle modifications and behavioral interventions for optimizing kidney health across the lifespan?
3. Which potential metrics are available now, and which are needed? This might include but are not limited to:
 - a. Process and adherence to recommended interventions
 - b. Patient reported outcome measures (PROMs)
 - c. Hard and soft clinical endpoints
 - d. Government and economic (e.g., employment, spending, healthcare price indexes, etc.)
 - e. Payer financial and quality metrics (e.g., per patient per month, HEDIS, NQF, etc.)
4. What data collection/access/infrastructure and privacy concerns must be addressed to establish benchmarks and track performance in these metrics?



- **Obtaining resources for implementation and showing cost effectiveness**
 1. Which audiences are interested in the cost effectiveness of a lifespan approach to kidney health, and for what reason(s)?
 2. How should cost-effectiveness data be used with these audiences to gain resources and support for implementation?
 3. What are the policy implications of adopting a lifespan approach to optimizing kidney health and diagnosing and managing kidney diseases?

- **Lessons and approaches gleaned from programs implementing CVD primary prevention: Emulating success and sidestepping failures**
 1. What are the opportunities for knowledge exchange and learning from other disciplines?
 2. Are there any examples of system-level primary prevention that have been implemented at scale that could be used to inform kidney health lifespan approaches?

- **How are we going to do it?**
 1. What are the key challenges and opportunities in coordinating care within a lifespan approach?
 - a. How can health systems be optimized to support this approach and ensure equitable access to care?
 2. What strategies can be employed to optimize care for individuals with multiple chronic conditions?
 - a. How can we tailor screening approaches to account for the lifespan perspective?
 - b. What are the potential benefits and challenges of implementing personalized strategies?
 3. What minimum financial resources, system structure, and local market conditions are necessary to implement a lifespan approach to kidney health?